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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,363	11/15/2001	Richard C. Duke	3923-3	2524

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/991,363	Applicant(s) DUKE ET AL.	
	Examiner Zachariah Lucas	Art Unit 1648	

-- Th MAILING DATE of this communication appears on the cover she t with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9-19-2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,9 and 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, and subgroups C and viii, and the species wherein the yeast vehicle is a whole yeast cell of a Saccharomyces yeast in Paper No. 13 is acknowledged. The traversal is on the ground(s) that there is no additional search burden in the examination of all of the claimed inventions of Groups I-II. This is not found persuasive because, as indicated in the restriction requirement, the searches required for each of these inventions are not coextensive with each other. Additional or different limitations are present in the different Groups/inventions such that a search for each of these inventions would be unduly burdensome.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 4-7, and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on June 27, 2002, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Priority

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) **in the first sentence of the specification** of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. While the present application does contain reference to the prior provisional application, the reference is not in the first sentence of the specification following the title.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, 3, 8, 9, 11-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions wherein the dendritic cells are loaded with either whole cell or spheroplast yeast vehicles and an antigen, does not reasonably provide enablement for therapeutic compositions wherein the dendritic cells is loaded with any yeast vehicle and an antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. These claims read on therapeutic compositions comprising a dendritic cell, a yeast vehicle, and an antigen. The Applicant has suggested that any

form of yeast vehicle that can be used with an antigen in a dendritic cell vaccine or as an adjuvant may be used in the claimed composition. Page 10, lines 21-23. Thus, the claims read broadly on dendritic cell vaccines comprising an antigen and any yeast vehicle.

However, in contrast to the breadth of the claims, the application provides only a single working example of a yeast vehicle that is capable of use in a dendritic cell vaccine. See, pages 35-44 (disclosing the examples of the application, each disclosing the use of only whole cell recombinant yeast vehicles). The Application indicates that it is the yeasts' cell wall components that are responsible, at least in part, for the ability of yeast cells to increase the DC ability to stimulate immune responses. Page 8, lines 14-20. While the specification teaches that yeast cell wall components are likely to be necessary for the operability for the claimed composition, the yeast vehicles identified by the Applicant, other than the whole cell vehicles, all lack the yeast cell wall. Page 10, lines 24-29. Thus, the teachings of the present application call in to question whether any yeast vehicle would be capable of activating dendritic cells.

It also noted, however, that a prior patent (Duke et al., U S Patent 5,830,463) teaches that spheroplasts, a cell wall lacking yeast vehicle, is capable of activating the cells. Cols 25-32. Thus, the teachings of the Duke patent indicate that some other feature of the yeasts allow the yeast vehicles to function. Because of the inconsistency between the teachings, it is not clear what the required features from the yeast cells are, and therefore the operability of the yeast vehicles other than the whole cell and the spheroplast comes in to question. Because of this uncertainty, and because the Applicant has not demonstrated that any yeast vehicle would be capable of inducing a therapeutic effect when administered to a DC in combination with an antigen, the Applicant is not enabled for compositions comprising any yeast vehicle.

Further, the claims also read on the claimed compositions wherein the compositions are therapeutically effective against any number different types of diseases. See e.g., claim 9, (indicating that the claimed composition can include antigens from a number of sources). However, the examples by the Applicant demonstrate indications that the claimed compositions were effective at inducing responses against only two sources. These examples include models of both cancer disorders and HIV infection. However, while the Applicant has demonstrated that the claimed compositions would be effective in the induction of some form of immune response in the recipient of the claimed compositions, the Applicant has not shown that the claimed compositions would be therapeutically active against any diseases caused by, or associated with, the identified antigenic sources. For example, Garber et al., AIDS Rev 5(3): 131-39 (teaching that while there has been success in the development of HIV vaccines, the current models of HIV are not necessarily predictive of the protective effects of the therapies). In combination with the teachings in the art that there is no model for HIV, it is also known in the art that treating HIV has been a generally complex and unpredictable technology. See e.g., Kaur et al., Top HIV Med, 11(3): 76-85, at 85 (teaching that although new approaches at therapeutic HIV vaccination have been tried, no clinical benefits have yet been realized). The art therefore indicates that, while the claimed compositions may be immunogenically effective against certain diseases, the therapeutic value of the claimed compositions has not been established against any of the identified diseases.

In view of the above, the Applicant is not enabled for therapeutic compositions comprising dendritic cells intracellularly loaded with any yeast vehicles and any antigen.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 6, 11, 13, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Sousa et al., J Exp Med 178(2): 509-19. This reference teaches the phagocytosis of Saccharomyces cerevisiae by isolated dendritic cells. The Applicant teaches that dendritic cells resenting an antigen are useful to induce immune responses, and that whole cell S. cerevisiae activate DC cells, and because a yeast cell inherently comprises antigens, the identified reference anticipates the identified claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 8, 9, and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Duke et al. (U.S. Patent 5,830,463- of record in the IDS of July 2002), in view of the teachings of Cohen et al. (U.S. Patent 6,187,307). These claims read on therapeutic compositions comprising a dendritic cell (DC), a yeast vehicle, and at least one antigen. The term yeast vehicle is being interpreted as comprising a particle composed of materials from a yeast

cell membrane. The particle may comprise the whole (intact or resealed) cell membrane, or may be, for example, a microparticle made from the sonication of the yeast membrane.

Duke teaches a yeast vehicle useful in therapeutic compositions. Abstract. The reference further teaches that these particles are efficient vehicles for transporting antigens to cells, including dendritic cells. Column 13, lines 36-53. The reference further teaches that the particles are effective in stimulating both humoral and cell-mediated immunity. Abstract, and column 18, lines 30-33. Among the discloses uses for the vehicle disclosed in the application is the delivery of the particles to cells in vitro, such that the particles can be absorbed by the cells, and the cells can then be returned to the animal from which they were isolated. Col. 19, lines 19-34. The reference teaches that such a method of delivery is useful in the induction of immune responses and in the treatment of tumors. Id. The reference does not however specifically teach the administration of therapeutic compositions comprising each of the dendritic cells, a yeast vehicle, and an antigen.

Cohen teaches the administration of a recombinant antigen-presenting cell (APC) to induce an immune response. Abstract, column 3, lines 36-60. The reference teaches immunogenic compositions comprising these cells, wherein the cells are transformed by, and express am antigen. Columns 3-4, claims 1-14. From the teachings of these references, it would have been obvious to those in the art to use the yeast vehicles of Duke to transform dendritic cells to become immunogenic, rather than use the recombinant or fusion techniques of Cohen, to create immunogenic cells. This is because, from the teachings of Duke, it would be apparent to those in the art that DC cells so treated would be capable of inducing the same, or similar responses as those created by the techniques of Cohen. The two patents differ in the mode of

inducing the cells to express the antigen against which an immune response is desired, but both relate to the same problem of creating immunogenic dendritic cells for to induce immune responses against a particular antigen, including tumor/cancer antigens. Because the two references are each concerned with the same problem, and because they teach alternative methods of creating cells with a similar function, those in the art would have had a reasonable expectation of success in combining the method of Duke for the introduction and activation of DC cells, with the method of Cohen to create immunogenic cellular compositions.

11. Claims 1, 2, 9, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Layton et al. (Immunol 87:171-78) and Adams et al. (Intern Rev Immunol 11:133-41) in view of the teachings of Tomai et al. (U.S. Patent 6,558,951). The claims have been described above.. As indicated above, the claims read on the use of any yeast vehicle. Such vehicles are described in the application as comprising any yeast vehicle "that can be used with an antigen in a dendritic cell vaccine or as an adjuvant." Page 10, lines 21-23. While the Applicant has provided examples (including subcellular yeast particles) of what may be included by the phrase "yeast vehicle," no other limitation on what may comprise a yeast vehicle has been provided. Thus, a yeast vehicle may be considered to include any particle that is derived from a yeast cell or that comprises yeast components.

Each of the Layton and Adams references teaches the use of yeast-derived virus-like particle (Ty particles) to deliver antigens to APC cells for the purpose of inducing a CTL immune response against the antigen. Abstracts. As indicated on page 172 of the Layton reference, these particles may be made by inserting a fusion polynucleotide (encoding a fusion

protein of the yeast p1 protein and one or more antigenic peptides) into a yeast cell, and isolating the VLPs from the yeast cell. Layton also teaches that the vehicles are effective for inducing responses against a plurality of antigens. Page 174. Thus, the references teach compositions comprising a yeast vehicle and an antigen for the delivery of antigens to a cell for therapeutic purposes. The references do not, however, teach a therapeutic composition comprising a dendritic cell that has been intracellularly loaded with the antigens.

Tomai teaches that matured DCs are can induce Th1 (CTL) responses. Column 1, lines 17-47. The reference also teaches that dendritic cells matured by the processes disclosed therein may be administered for the treatment of diseases upon exposure to an antigen. Col 15, lines 4-55, esp. lines 34-41. From this reference, those in the art would have had adequate motivation to load DC cells with a desired antigen. This is because Tomai teaches the loading of DCs with desired antigens; and Adams and Layton teach that the Ty particles are effective at delivering antigenic peptides to immune cells. These teachings both render obvious, and provide motivation, to those in the art for the loading of the DC cells of Tomai with the antigen compositions of Layton or Adams.

As the Layton and Adams references indicate that the Ty particles effectively induce immune responses, it would be apparent to those in the art that such particles could be processed by the dendritic cells and presented on appropriate MHC complexes. Thus, those in the art would have had a reasonable expectation of success in the combination of the references.

12. Claims 1-3, 8, 9, and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Duke in view of the teachings of Tomai. The claims have been described

above, as have the teachings of the identified references. From these references, it would have been obvious to those in the art to use the antigenic particles of Duke to activate the DC cells of Tomai. Because Tomai teaches the DCs may also be contacted with antigens generally, and as it would have been obvious to those in the art to combine compositions that perform the same function, it would also have been obvious to those in the art to load the DCs of Tomai with both the yeast particles of Duke and with free antigen. Further, because Duke teaches that the particles disclosed therein have immunopotentiating activity, those in the art would both have been motivated to mix the antigens with the particles, and have had a reasonable expectation of success in the combination.

Conclusion

13. No claims are allowed.

14. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Paglia et al., J Exp Med, 183 : 317-22. This reference teaches that dendritic cells loaded with proteins in vitro were capable of inducing immune responses when the cells were re-introduced into an animal. Abstract. However, the reference does not teach the use of a yeast vehicle to introduce antigens into the dendritic cell, or the use of dendritic cells that have been intracellularly loaded with such vehicles and an antigen.
>
> Allsopp et al., Eur J Immunol, 26 : 1951-59. This reference is considered redundant to the teachings of Adams and Layton as described above. See e.g., Allsopp, page 1955.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner

12/1/03

JAMES HOUSEL
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